

### **Listing of Claims**

The following list of claims will replace all prior versions and listings of claims in the application.

1. (Currently Amended) A nucleic acid construct comprising ~~a nucleic acid sequence further comprising~~ a nucleic acid sequence encoding a secretable or excretable reporter protein and an inducible promoter that drives the production or expression of said reporter protein. ~~that is secretable or excretable as a protein or product from a cell where the protein or product is expressed or produced.~~
2. (Currently Amended) The nucleic acid construct according to claim 1, wherein the production or expression of the secretable/excretable protein or product is mediated ~~produced~~ by modulated gene transcription.
3. (Currently Amended) The nucleic acid construct according to claim 1, wherein the production or expression of the secretable/excretable protein or product is mediated ~~produced~~ by increased reporter translation.
4. (Previously Presented) The nucleic acid construct according to claim 3, wherein the increased reporter translation is a function of increased stability or decreased turnover of mRNA.
5. (Currently Amended) The nucleic acid construct according to claim 1, wherein the production or expression of the secretable/excretable protein or product is mediated ~~produced~~ by post-translational modulation.
6. (Previously Presented) The nucleic acid construct according to claim 5, wherein the post-translational modulation is increased reporter stability through removal of polyubiquitination or a function of accumulation or excretion of small molecule metabolites.

7. (Previously Presented) The nucleic acid construct according to claim 37, wherein the peptide tag further comprises an epitope tag or a tag comprising enzymatic activity.

8. (Previously Presented) The nucleic acid construct according to claim 37 further comprising a promoter element upstream of (i) the nucleic acid sequence encoding the secreted/excreted protein, and/or (ii) a nucleic acid sequence encoding the peptide tag.

9. (Withdrawn) The nucleic acid construct according to claim 1, wherein the secreted/excreted reporter protein is secreted alkaline phosphatase (SEAP).

10. (Withdrawn) The nucleic acid construct according to claim 9, wherein the construct further comprises a CypA1 promoter.

11. (Previously Presented) The nucleic acid construct according to claim 1, wherein the secreted/excreted reporter protein is a modified human  $\beta$  choriogonadotrophin (hCG) molecule.

12. (Previously Presented) The nucleic acid construct according to claim 11, wherein the construct further comprises a stratifin gene promoter.

13. (Previously Presented) The nucleic acid construct according to claim 11, wherein the hCG molecule is tagged.

14. (Previously Presented) The nucleic acid construct according to claim 13, wherein the hCG molecule is myc-tagged.

15. (Previously Presented) The nucleic acid construct according to claim 1, wherein the secreted/excreted reporter protein/product is selected from the group consisting of hormonal molecules, antibodies and enzymatic molecules.

16. (Withdrawn) The nucleic acid construct according to claim 15, wherein the hormonal molecule is FSH.

17. (Withdrawn) The nucleic acid construct according to claim 15, wherein the antibody is a  $\gamma$  or light chain (Bence Jones) protein.

18. (Withdrawn) The nucleic acid construct according to claim 15, wherein the enzymatic molecule is feline urinary carboxylase.

19. (Previously Presented) A host cell comprising at least one nucleic acid construct according to claim 1.

20. (Previously Presented) A cell line comprising at least one nucleic acid construct according to claim 1.

21. (Previously Presented) A transgenic non-human animal wherein the cells of the non-human animal express the protein or product encoded by the nucleic acid sequence of the nucleic acid construct according to claim 1.

22. (Previously Presented) The transgenic non-human animal according to claim 21, wherein the non-human animal is a mammal.

23. (Previously Presented) The transgenic non-human mammal according to claim 22, wherein the mammal is a mouse.

24. (Previously Presented) The transgenic non-human animal according to claim 21, wherein the secreted/excreted reporter protein or product is excreted in a body fluid selected from the group consisting of urine, saliva, tears, milk, cerebrospinal fluid and semen.

25. (Previously Presented) The transgenic non-human animal according to claim 21, wherein the secreted/excreted reporter protein or product is excreted in urine.

26. (Previously Presented) The host cell according to claim 19, wherein the secreted/excreted reporter protein or product has a molecular weight of about less than 60-120kDa.

27. (Previously Presented) The host cell according to claim 19, wherein the secreted/excreted reporter protein or product comprises a hydrophilic globular tertiary structure, low bio-activity and/or is distinguishable from endogenous molecules.

28-30. (Canceled)

31. (Currently Amended) A method of detecting a gene activation event ~~in a cell~~ *in-vitro or in-vivo*, comprising assaying a host cell or transgenic non-human animal, wherein:  
(i) the host cell or transgenic non-human animal comprises each comprising a  
nucleic acid construct according to claim 1, wherein  
(i) the host cell or transgenic non-human animal is subjected to a gene  
activation event, and  
(iii) the occurrence of the gene activation event is signaled that is signalled by  
expression of a secreted/excreted the secretable or excretable reporter protein  
wherein the protein is optionally tagged with an epitope.

32. (Currently Amended) A method of screening for, or monitoring of, toxicologically induced stress ~~in a cell or a cell line or a transgenic non-human animal,~~ comprising evaluating a cell, a cell line or a transgenic non-human animal, wherein:  
(i) the cell, cell line or transgenic non-human animal comprises a each  
comprising the nucleic acid construct according to claim 1, and  
(ii) toxicologically induced stress is signaled by expression of the secretable or  
excretable reporter protein.

33. (Currently Amended) A method for screening and characterizing viral, bacterial, fungal, and parasitic infection, or for screening for cancer, inflammatory disease, cardiovascular disease, metabolic disease, neurological disease and disease with a genetic basis comprising evaluating a cell, a cell line or a transgenic non-human animal, wherein:

(i) the cell, cell line or transgenic non-human comprises a ~~each comprising the~~ nucleic acid construct according to claim 1, and

(ii) infection, cancer and disease are signaled by expression of the secretable or excretable reporter protein.

34. (Previously Presented) The nucleic acid construct according to claim 1, wherein the reporter protein is expressed or produced in vitro or in vivo.

35. (Previously Presented) The nucleic acid construct according to claim 1, wherein the reporter protein is secretable/excretable from a whole animal.

36. (Previously Presented) The nucleic acid construct according to claim 35, wherein the whole animal is a transgenic non-human animal.

37. (Previously Presented) The nucleic acid construct according to claim 1, wherein the construct further comprises a peptide tag.

38. (Previously Presented) A reporter system comprising at least two nucleic acid constructs, wherein the nucleic acid constructs each comprise:

(i) a nucleic acid sequence encoding a reporter protein; and

(ii) a nucleic acid sequence encoding a peptide tag to the reporter protein,

wherein each reporter protein is distinct from the proteins normally expressed in the host comprising the reporter system.

39. (Previously Presented) The reporter system according to claim 38, wherein the at least two nucleic acid constructs encode a same reporter protein having a different peptide tag or encode a different protein having a same peptide tag.

40. (Withdrawn) The reporter system according to claim 38, wherein the reporter protein is selected from the group consisting of secreted alkaline phosphatase (SEAP), a  $\gamma$  or light chain (Bence Jones) protein and feline urinary carboxylase.

41. (New) A nucleic acid construct comprising a nucleic acid sequence encoding a secretable or excretable reporter protein, wherein said reporter protein is produced or expressed as a result of one or more of the following:

- (i) disturbances in the homeostatic state of DNA;
- (ii) oxidative stress or hypoxia;
- (iii) hepatotoxic stress;
- (iv) presence of a pro-apoptotic stimulus;
- (v) administration of chemical, drugs, or other xenobiotic agents;
- (vi) disease onset, either natural, modeled or induced.

42. (New) The nucleic acid construct of claim 41, wherein the construct further comprises a peptide tag.